Epidemiology and Comorbidity of Erysipelas in Primary Care

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Key Words

Erysipelas, epidemiology • Erysipelas, comorbidity • General practice

Abstract

Background/Aims: Most studies on the epidemiology of erysipelas are done in hospitals, resulting in patient selection. The aim of this study is to determine epidemiological characteristics and comorbidity of erysipelas based on primary care data. **Methods:** Incidence rate study and nested case-control study. A database containing data from 52 general practices in Flanders, Belgium, with morbidity data on 160,000 different patients in the period 1994–2004. Excess comorbidity was determined in patients with erysipelas in 2004. **Results:** In the period 1994–2004, the age-standardized incidence of erysipelas increased significantly from 1.88 (95% confidence interval, CI, 1.62–2.13) per 1,000 patients to 2.49 (95% CI 2.24–2.74). Of patients with erysipelas, 16% had one or more recurrences. Local factors such as dermatophytosis, chronic ulcer of the skin, varicose veins of the leg and phlebitis and general disorders such as obesity, non-insulin-dependent diabetes and heart failure increased the risk of erysipelas. **Conclusion:** The incidence of erysipelas increased from 1994 to 2004. More attention should be paid to local factors such as dermatophytosis to prevent erysipelas.

Objective

Despite the relative frequency of erysipelas, information on the incidence and the basic epidemiological characteristics of this disease is scarce. There are only a few recent epidemiological studies [1–3] and those were all undertaken in hospital settings despite the fact that this disease is mostly treated in primary care.

Erysipelas or St. Anthony's fire [4] is a serious infectious disease that starts with high fever and general illness without specific signs. After 1 day, localized erythema appears on the legs or more rarely in the face or somewhere else. There are no specific tests for the diagnosis, which is based on clinical findings. Erysipelas is caused by *Streptococcus pyogenes* but the bacteriological diagnosis remains difficult [5]. Treatment with antibiotics is effective and does not normally cause difficulties. That is why the disease can be completely diagnosed and treated in general practice and referral to a specialist will rarely be necessary [6]. It is an annoying disease for the patient as it frequently recurs; percentages of recurrences vary from 23.5% [7] to 29% [8]. These recurrences affect the lymphatic vessels so that lymphatic draining progressively deteriorates after each recurrence.

In the 1970s the idea existed that antibiotics had conquered the streptococcal infections [9], but at the end of

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the eighties streptococcal infections with serious complications reappeared. Two French studies [3, 10] described a progressive increase in the yearly number of hospitalizations for erysipelas between 1978 and 1991 and between 1959 and 1995.

In the Continuous Morbidity Registration in the Netherlands [6] based on registration in general practice, the incidence rate of erysipelas was at its lowest ebb in 1992 of 1.5 per 1,000 patient-years with an increase to 3.0 per 1,000 patient-years in 1999.

No significant difference between the sexes has been found in the past. There are different opinions on seasonal variation: some studies describe an increased incidence in spring and autumn [7], another study found no seasonal variation [8] and in recent studies an increased frequency was seen in summer [2, 11].

Studies that examined the influence of risk factors also showed different results. Local predisposing factors such as lymphedema, leg ulcer and venous insufficiency are identical in most studies [12]. Jorup-Rönström [8] and Crickx et al. [7] found alcohol abuse and diabetes as general predisposing factors. This finding was not confirmed in two case-control studies [2, 13].

The lack of recent epidemiological data on erysipelas based on the general population makes it difficult to draw conclusions about epidemiological figures. The necessity of community-based studies has therefore been emphasized [1, 2, 13]. This study examines the incidence, determinants and comorbidity of patients with erysipelas based on primary care data.

Method

The Intego Database

Data were obtained from the Intego database [14]. This database is composed of data from primary care in Flanders as well as the northern part of Belgium and updated annually. Registration in the practices is performed via the electronic medical record Medidoc™, which is a strongly structured program. Only general practices with data of sufficient quality are imported into the database. GPs get tips for registering and specific training in workshops. The data are regularly submitted to internal quality controls. The number of registering practices increased from 26 (34 doctors) in 1999 to 52 (67 doctors) in 2004 and there are almost no omissions of co-operating practices. The population of the database is comparable to the Flemish population, and the practices are spread over the whole of Flanders. GPs note diagnoses by means of software-specific key words, which they select from a list of 27,000. In the central database these keywords are converted into the ICPC-2 classification. The Intego database contains information on 740,000 patient-years of 160,000 different patients for whom in the period 1994–2004 more than 1,500,000 diagnoses were made. No formal criteria are used for

the recording of diagnoses in the doctor's electronic medical record. Every doctor is free to determine on which grounds he decides to make and record the diagnosis of erysipelas.

The incidence is the number of diagnoses of erysipelas calculated per 1,000 patients during a year in the period 1994–2004. It does not necessarily concern first episodes of the disease. The incidences are age standardized according to the Flemish population of January 1, 2000.

To examine the seasonal variation, the relative frequency of the number of diagnoses of erysipelas for the years 2002–2004 was calculated per month and compared to the total number of diagnoses.

Comorbidity described at least once in the literature was examined in all patients with a diagnosis of erysipelas in 2004 and compared with patients who had never been affected by erysipelas and contacted the practice in 2004. At the same time the comorbidity of patients who were only once affected by erysipelas was compared to those who had recurrences. A patient is labeled with a disease, if the diagnosis is recorded at least once in his medical history. The Intego database does not contain lifestyle information such as alcohol use or smoking behavior.

Ethics

The Intego project was presented to the Belgian Privacy Commission and approved by the Ethical Review Board of the Medical School of the Katholieke Universiteit Leuven.

Statistics

For the calculation of the 95% confidence intervals (CI) in the age-standardized incidences and in the different age groups, the statistical program Confidence Interval Analysis [15], version 2.1.1, was used. To calculate the 95% CI of the incidence ratio, the formula [16] $e^{\ln RR \pm 1.96 \sqrt{1/A_1 + 1/A_0}}$ was used, where A_1 and A_0 are the number of patients with the disease in 1994 and 2004, respectively.

The odds ratios (OR) of the comorbidity proportions with their 95% CI and χ^2 or Fisher's exact tests were calculated by the statistical program SPSS 12.0 for Windows™.

Results

Incidence

The yearly age-standardized incidence of erysipelas increased from 1.88 per 1,000 patients in the years 1994–1995 to 2.49 in 2003–2004. The incidence ratio in 2003–2004 compared to 1994–1995 was 1.32 (95% CI 1.12–1.56; tables 1 and 2). Erysipelas is a disease that particularly occurs in a higher age bracket. An increase occurs in the three highest age groups but is only significant in the 75+ age group with an incidence ratio of 2.19 (95% CI 1.39–3.44; table 2). The incidence in men and women did not differ significantly during the 11-year period (data not shown).

Erysipelas was significantly more frequent in the summer months June, July and August and less frequent in

Table 1. Incidence of erysipelas per 1,000 patient-years from 1994 to 2004, standardized by age

Year	Total		Females		Males	
	n	incidence, ‰	n	incidence, ‰	n	incidence, ‰
1994	100	1.74 (1.39–2.08)	61	2.07 (1.51–2.62)	39	1.42 (0.88–1.97)
1995	119	2.00 (1.64–2.37)	57	1.86 (1.19–2.52)	62	2.19 (1.59–2.78)
1996	134	2.19 (1.77–2.61)	71	2.28 (1.59–2.97)	63	2.13 (1.53–2.74)
1997	148	2.34 (1.92–2.77)	81	2.51 (1.85–3.16)	67	2.15 (1.55–2.74)
1998	115	1.71 (1.38–2.05)	62	1.83 (1.32–2.34)	53	1.64 (1.1–2.18)
1999	136	2.02 (1.66–2.38)	71	2.08 (1.57–2.56)	65	1.99 (1.43–2.55)
2000	160	2.13 (1.78–2.48)	82	2.11 (1.63–2.60)	78	2.21 (1.55–2.86)
2001	172	2.34 (1.97–2.71)	94	2.44 (1.80–3.09)	78	2.32 (1.74–2.9)
2002	168	2.19 (1.81–2.57)	80	1.98 (1.46–2.51)	88	2.47 (1.83–3.1)
2003	205	2.55 (2.19–2.9)	100	2.37 (1.87–2.86)	105	2.78 (2.21–3.35)
2004	199	2.43 (2.06–2.79)	100	2.41 (1.87–2.95)	99	2.52 (1.98–3.07)

Figures in parentheses indicate 95% CI.

Table 2. Incidence of erysipelas by age group per 1,000 patient-years in 1994–1995 and 2003–2004

Age group	1994–1995		2003–2004		Incidence ratio
	n	incidence rate	n	incidence rate	
25–44 years	63	1.63 (1.25–2.09)	77	1.90 (1.50–2.37)	1.17 (0.84–1.63)
45–64 years	82	2.97 (2.36–3.68)	137	3.53 (2.96–4.18)	1.19 (0.90–1.56)
65–74 years	32	2.89 (1.98–4.08)	63	4.14 (3.18–5.30)	1.43 (0.94–2.19)
≥75 years	23	3.11 (1.97–4.67)	101	6.80 (5.53–8.26)	2.19 (1.39–3.44)
Total	219	1.88 (1.62–2.13)	404	2.49 (2.24–2.74)	1.32 (1.12–1.56)

Younger age groups are not shown because of the low numbers. Figures in parentheses indicate 95% CI.

the winter months December, January and February (data not shown).

During the period 1994–2004, 1,656 cases of erysipelas were diagnosed in 1,336 different patients. In 1,125 patients (84%), the disease occurred only once and 211 patients (16%) had one or more recurrences (table 3). The proportion of recurrences did not change across the age groups.

Comorbid Diseases Related to Occurrence

In the 45- to 64-year age group, only dermatophytosis (OR 1.88), chronic skin ulcer (OR 7.34) and obesity (OR 4.10) were significantly more frequent in patients with erysipelas compared to those without the disease. In the age group 65+, heart failure (OR 2.91), phlebitis and thrombophlebitis (OR 3.62), varicose veins of the legs (OR 1.86), dermatophytosis (OR 2.41), chronic skin ulcer (OR 4.52) and non-insulin-dependent diabetes mellitus (OR 2.78) were significantly more frequent (table 4).

Table 3. Number of episodes of erysipelas per patient from 1994 to 2004

Number of cases per patient	Number of patients	Percent of total
1	1,125	84.21
2	150	11.23
3	36	2.69
4	14	1.05
5	5	0.37
6	4	0.30
≥7	2	0.14
Total	1,336	100

Comorbid Diseases Related to Recurrence

Local diseases were more frequent in patients with recurrences of erysipelas compared to those without. In the 45- to 64-year age group only dermatophytosis (OR 4.24)

Table 4. Comorbidity of patients with erysipelas and with recurrent erysipelas and their OR with 95% CI in parentheses

ICPC code and title	Age group	Patients with erysipelas		Patients without erysipelas		OR	Patients with recurrent erysipelas		Patients without recurrent erysipelas		OR
		n	%	n	%		n	%	n	%	
K77 heart failure	45–64	0	0	0	0		0	0	0	0	
	≥65	9	11.54	634	4.29	2.91 (1.45–5.86)*	4	18.18	5	8.93	2.27 (0.55–9.38)
K94 phlebitis and thrombophlebitis	45–64	4	6.67	711	3.73	1.84 (0.67–5.09)	2	10.53	2	4.88	2.29 (0.3–17.66)
	≥65	18	23.08	1,131	7.65	3.62 (2.13–6.15)*	9	40.91	9	16.07	3.62 (1.19–10.96)*
K95 varicose veins of leg	45–64	5	8.33	1,238	6.5	1.31 (0.52–3.27)	1	5.26	4	9.76	0.51 (0.05–4.94)
	≥65	13	16.67	1,434	9.7	1.86 (1.02–3.38)*	6	27.27	7	12.5	2.63 (0.77–8.96)
S74 dermatophytosis	45–64	14	23.33	2,654	13.94	1.88 (1.03–3.42)*	8	42.11	6	14.63	4.24 (1.21–14.91)*
	≥65	17	21.79	1,531	10.36	2.41 (1.41–4.14)*	7	31.82	10	17.86	2.15 (0.69–6.63)
S97 chronic skin ulcer	45–64	2	3.33	89	0.47	7.34 (1.77–30.52)*	1	5.26	1	2.44	2.22 (0.13–37.55)
	≥65	10	12.82	466	3.15	4.52 (2.31–8.83)*	6	27.27	4	7.14	4.88 (1.22–19.45)*
T82 obesity	45–64	9	15	785	4.12	4.10 (2.01–8.36)*	6	31.58	3	7.32	5.85 (1.28–26.79)*
	≥65	5	6.41	491	3.32	1.99 (0.80–4.95)	3	13.64	2	3.57	4.26 (0.66–27.50)
T90 diabetes, non-insulin-dependent	45–64	4	6.67	886	4.65	1.46 (0.53–4.04)	2	10.53	2	4.88	2.29 (0.30–17.66)
	≥65	20	25.64	1,630	11.03	2.78 (1.67–4.64)*	7	31.82	13	23.21	1.54 (0.52–4.59)

* Statistically significantly different.

was significantly more frequent. In the 65+ age group only phlebitis and thrombophlebitis (OR 3.62) and chronic skin ulcer (OR 4.88) were significantly more frequent (table 4).

Conclusion

The increase in the sex-specific and age-adjusted incidence of erysipelas is around one third over 10 years and occurs especially in the 75+ age group. There is no obvious direct explanation for this increase. The disorder is recurrent in 16% of patients.

Local diseases such as dermatophytosis, chronic ulcer of the skin, phlebitis and varicose veins seem to increase the risk of erysipelas, usually at a higher age. Additionally, non-insulin-dependent diabetes, obesity and heart failure increase the risk. The small difference in comorbidity between patients with or without recurrences of erysipelas is striking. Only local diseases such as dermatophytosis, phlebitis and chronic ulcer of the skin are more frequent in patients with recurrences, but CI are wide.

The question is asked whether the increased incidence of erysipelas relates to the increase in group A streptococcal infections [9]. Recently also *Staphylococcus aureus* has been isolated from lesions from bullous erysipelas and the question is whether this bacterium plays an etiological part or whether it is rather a contaminant [17, 18].

Such an increase may be the result of decreased host immunity or increased virulence of the bacteria. As it is difficult to make a bacteriological diagnosis of erysipelas [19], it would be interesting to have access to bacteriological samples originating from primary care-based cases, but this is not possible at the moment. It would also be interesting to examine whether a relapse is caused by the same serological type or whether reinfection occurs with a strain of a different serotype [20].

The percentage of recurrences in our study (16%) is lower than the percentages (29, 30%) reported in earlier studies [1, 8]. This can be explained by the bias of hospitalized patients in these former studies, because more serious and progressing cases were seen in hospital.

In our study an increase in the incidence of erysipelas during the summer months and a decrease during the winter months was obvious. This contrasts with infections of the upper respiratory system, which occur more frequently in the winter months. A relation with streptococcal pharyngitis, as was suggested in former studies, is therefore probably unlikely [7, 8].

Varying comorbidities have been described. Our results correspond to those of hospital-based studies [1, 2, 7, 11]. These authors found venous insufficiency, lymphedema and toe-web intertrigo caused by fungal infection in almost all cases. Disruption of the cutaneous barrier by a leg ulcer or wound also resulted in an increased risk. Of the general factors, in some studies diabetes [7, 8] was a risk factor and in others obesity [2, 11]. This picture of

various comorbidities may result from the heterogeneous composition of the population examined in the hospital settings, the absence of age stratification or the combination of diabetes type I or II in earlier studies.

The risk factors in the patient group with recurrent erysipelas differ little from the group with only one episode as also described by Leclerc et al. [21]. Like Pavlotsky et al. [11], we found a higher frequency of obesity and dermatophytosis in the group of patients with more episodes.

In the Intego project every doctor makes a diagnosis on clinical grounds, whether or not assisted by further investigations. No formal diagnostic criteria are used. The doctor decides independently on which grounds he notes the diagnosis in the medical record. This is no real problem for erysipelas, since it is a clinical diagnosis, only based on the history and the clinical findings. It may however influence the detection of some of the comorbidities. Lifestyle factors such as smoking habits, alcohol use and hygiene are not recorded.

This investigation is based on data from a continuous registration network in primary care and therefore responds to the criticism that has been leveled against hospital-based studies of erysipelas [1, 2, 13].

Because local factors may result in an increased risk of occurrence of erysipelas, it is important to pay sufficient attention to these local diseases in patients with a general predisposition (e.g. the obese or patients with a chronic disease). It is possible that aggressive therapy for common infections such as dermatophytosis might have a positive preventive effect on the occurrence of this serious infection.

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